Paper No. 34

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte TIMOTHY W. NILSEN, HUGH D. ROBERTSON,
and THOMAS J. KINDT

Appeal No. 2003-1792
Application No. 09/434,598

ON BRIEF

Before WINTERS, SCHEINER, and MILLS, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 34-37which are all of the claims pending in this application.

Claim 37 is illustrative of the claims on appeal and reads as follows:

37. A set of affector oligomers for specifically reducing the expression of an RNA molecule of interest, wherein each oligomer is an external guide sequence specifically guiding cleavage of an RNA molecule of interest by RNAse P under in vivo conditions, wherein each oligomer is targeted to a site on the RNA molecule of interest, or to a site in a portion of a first reporter gene encoding the RNA molecule of interest, wherein the oligomers collectively are targeted to all or a substantial number of the accessible sites in the RNA molecule of interest as identified by

(a) introducing into cells a set of nucleic acid molecules,

wherein, after introduction of the nucleic acid molecules, each cell comprises the first reporter gene, a second reporter gene, and a targeting gene, wherein the first reporter gene encodes a fusion protein comprising a protein of interest and a first reporter protein, wherein the second reporter gene encodes a second reporter protein, wherein the protein of interest is encoded by the RNA of interest, wherein the targeting gene encodes an affector RNA molecule comprising a targeting sequence, wherein each nucleic acid molecule in the set is the same except for the encoded affector RNA molecule, wherein (1) the affector RNA molecule encoded in each nucleic acid molecule in the set is targeted to a different site on the RNA molecule of interest or to a different site in the portion of the first reporter gene encoding the RNA molecule of interest, or (2) the targeting sequence of the affector RNA molecule in each nucleic acid molecule is degenerate or partially degenerate,

(b) identifying those cells from step (a) that both express the second reporter protein and exhibit reduced expression of the first reporter protein, and

(c) identifying the affector RNA molecules encoded by the nucleic acid molecules present in the cells that both express the second reporter protein that exhibit reduced expression of the first reporter protein.

The prior art references cited by the examiner are:

George et al (George)[1] WO 96/21731 July 18, 1996

Milligan et al. (Milligan),"Current Concepts in Antisense Drug Design," J. of Med. Chem., Vol. 36, No. 14, pp. 1923-1937 (1993)

Grounds of Rejection

Claims 34, 35 and 37 stand rejected under 35 U.S.C. §102(b), as anticipated by George.

Claim 36 stands rejected under 35 U.S.C. §103(a), as obvious over George in view of Milligan.

We affirm these rejections.

Claim Grouping

[1] Throughout the prosecution history, the examiner mistakenly refers to this publication as Shaji, et al. We refer to this international publication by its appropriate first author, as "George."

We do not find that appellant's claim grouping conforms with Rule 1.192. While appellants have grouped claims 34 and 35 separately from claim 37 (Brief, page 4), they have not presented separate argument as to why claims 34 and 35 are patentable in view of the cited art. Since the individual claims of each group are not argued, we decide this appeal with respect to the prior art rejections on the basis of claim 37, as representative of Group I, and claim 36, as representative of Group II. Thus, claims 34 and 35 fall with claim 37. 37 CFR §1.192(c)(7) (2002).

DISCUSSION

Background

The claimed invention is directed to a set of affector oligomers for specifically reducing the expression of an RNA molecule of interest. Affector RNA molecules include ribozymes, external guide sequences, anti-sense RNA and triple helix forming RNA that inhibit expression of target RNA molecules. Specification, page 1.

Disclosed in the specification is a method of identifying affector molecules by screening or selecting for those RNA molecules that alter the expression of a fusion transcript which includes the sequence of an RNA molecule of interest, from a library of potential affector RNA molecules. Specification, page 8. Inhibition of expression of the fusion transcript prevents expression of the reporter protein. This allows inhibition of expression to be monitored by detecting expression of the reporter protein. Id. The inhibition of expression is accomplished by interaction of a nucleic acid molecule involved in the expression of the RNA molecule of interest with an affector molecule.

Ribozymes and external guide sequences result in cleavage of the fusion transcript, and antisense RNA and triple helix-forming RNA block expression through hybridization to a nucleic acid molecule involved in the expression of the fusion transcript. Id. Inhibitory oligomers are based on affector molecules identified as altering the expression of an RNA of interest. Specification, page 9.

An example of an external guide sequence is a sequence for promoting cleavage by eukaryotic RNAse P, and the external guide sequence contains sequences which are complementary to the target RNA and which forms secondary and tertiary structure akin to portions of a tRNA molecule. Specification, page 20.

The specification states that an advantage of the "disclosed method is that all, or a substantial number of accessible sites in the RNA of interest can be determined in one assay. Such sites, determined to be accessible for one type of affector molecule, may be accessible for other types of affector molecules. In the case of ribozymes and external guide sequences, the disclosed method allows assessment not just of cleavage of the RNA of interest, but also of an ultimate desired phenotype (that is, loss of the phenotype supported by the RNA of interest) as a result of such cleavage." Specification, page 9.

35 U.S.C. §102(b) and §103(a)

Claims 34, 35 and 37 stand rejected under 35 U.S.C. §102(b), as anticipated by George. Claims 36 stands rejected under 35 U.S.C. §103(a), as obvious over George in view of Milligan.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

It is the examiner's position that George (Answer, page 4):

> disclose 80 EGS [external guide sequences] (a set) that have been screened by methods disclosed in the reference. In Example 6 ...[George] disclose that from the screening it was determined two distinct regions that represented accessible target regions. Twelve (a set) of the EGSs were then chemically modified and tested further.

We find no error in the examiner's determination that George anticipates the claimed invention within the meaning of 35 U.S.C. 102(b).

Appellants argue that George (Brief, page 10):

> differs from the claimed set of oligomers in two features:
>
> 1) not all of the EGS of Shaji [George] are functional, in contrast to the claimed set, which by virtue of the method of manufacture and selection, must all be functional; and
> (2) not all of the EGSs of Shaji [George] are "targeted to all or a substantial number of the accessible sites in the RNA molecule of interest."

The examiner counters the appellants' position, arguing (Answer, page 6)

> It is clear that at least the 12 EGS of Shaji et al represent a set of

> functional EGS since these were all shown to have activity, for example. Appellant argues that these could not represent EGS targeting a substantial number of sites. It is noted however that the specification and applicant arguments fail to provide specifically what constitutes a substantial number... It is the position of the examiner that the 12 functional EGS of Shaji [George] et al would clearly represent a substantial number. It appears that applicant admits on page 10 of the Brief that the 12 EGS of Shaji [George] et al could be identified by the instantly claimed method but then argue again that this would not constitute a substantial number or "sufficient "coverage' of accessible sites."

In the Answer, the examiner also quotes a passage from the prosecution history, an Office Action mailed 2/12/02. In that Office Action the examiner states (Answer, page 7):

> Applicant argues that the amendments... overcome the prior art since the prior art does not teach a set of EGS that target all or a substantial number of accessible sites on a target RNA. First the instant claims are not so limited. The instant claims only require that the set of EGSs collectively target all or a substantial number of the accessible sites in a target RNA as identified by the method. In other words, if one in the art tested two EGS in applicants' methods and found two that work the resulting set now represents all and a substantial number of accessible sites as identified in the method. Therefore the set of EGS disclosed by Shaji [George] et al would collectively target all the accessible target sites of a target RNA identified using the methods disclosed in Shaji [George] et al and in the method of the instant invention. [Emphasis original.]

We see no error in the examiner's characterization of George and its relevance to claim 37.

Appellants argue that the "80EGS of Shaji are not encompassed by the currently pending claims." Brief, page 9. However the appellants have not adequately addressed the examiner's argument that the 12 EGS of George are encompassed by the currently pending claims, and have been determined by George to be a functional

set which may be further used to analyze RNA.

With respect to appellants' argument that not all of the EGSs of Shaji [George] are "targeted to all or a substantial number of the accessible sites in the RNA molecule of interest" in our view the examiner has provided a reasonable analysis in the Answer as to why one of ordinary skill in the art would have understood the EGS of George are directed to a substantial number of accessible sites in the RNA molecule of interest. The examiner finds that the "specification and applicant[s'] arguments fail to provide what specifically constitutes a substantial number..." Answer, page 6. We agree and therefore attribute the ordinary meaning to the term "substantial" in the claims. [2] In addition, under such circumstances, the PTO can require an applicant to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical. See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). While "indirect comparisons, based on established scientific principles, can validly be applied to distinguish a claimed chemical process or product from that disclosed in the prior art," In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 432 (CCPA 1977), the comparisons must be scientifically valid.

Appellants' burden under the circumstances presented herein was described in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

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[2] The term "substantial" is defined in Miriam Websters on-line dictionary as "being largely but not wholly that which is specified."

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

In the present case we find that the examiner has presented sufficient argument and evidence to support the position that the claimed affector molecules are the same or substantially the same as the prior art 12 identified EGS. Thus, the burden shifts to appellants to show that the prior art affector oligomers do not possess the claimed characteristics of targeting a substantial number of sites on a target DNA and full functionality. This appellants have not done.

Appellants also argue that only 12 of the 80 EGS induced in vitro cleavage and that the claims are drawn to in vivo cleavage. Brief, page 9; Answer, page 6. The examiner responds, noting that one would of ordinary skill in the art would have expected all of the EGS to function in vivo as they were observed to function in vitro, and that appellants' examples were also performed in vitro. Answer, page 6. We do not find appellants have presented argument as to why one of ordinary skill in the art would not have expected the results of in vitro testing of George to be correlated to those of in vivo testing.

Furthermore, it is unclear from the record whether the appellants relied on the product by process language set forth in claim 37 for patentability of the claim. To the

extent that such a reliance is made, the examiner indicates on page 6 of the Answer, that "applicant admits on page 10 of the Brief that the 12 EGS of Shaji [George] et al could be identified by the method instantly claimed..."

While appellants have grouped claims 34 and 35 separately from claim 37, they have not presented separate argument as to why claims 34 and 35 are patentable in view of the cited art. The rejection of claim 37 under 37 U.S.C. § 102(b) is affirmed. Dependent claims 34 and 35 fall with claim 37.

Claim 36

Claim 36 stands rejected under 35 U.S.C. § 103(a), as obvious over George in view of Milligan.

Milligan is relied on by the examiner for the disclosure of peptide nucleic acid (PNA) modifications that provide for nuclease and target affinity which can be used in antisense molecules and have taught the advantages of these modifications in antisense technology. Answer, pages 4-5.

The examiner concludes (Answer, page 5)

> It would have been obvious for one of ordinary skill in the art to modify the EGS molecules taught by Shaji [George] et al with the PNA modifications taught by Milligan et al since Shaji et al have taught numerous modifications for increasing target affinity and for providing nuclease resistance and the importance of such characteristics. One of ordinary skill, based on the teachings of Shaji et al in regard to the desirability to modify EGS and their teachings of how and where such desirable modifications can be made in such a molecule, would have expected success in modifying EGS molecules with PNA since Milligan et al have taught the benefits of such modifications in regard to stability and increased target affinity.

Appellants argue, “there is a distinction between an antisense mechanism of gene expression inhibition and an EGS mediated form of gene expression inhibition ...wherein an antisense RNA blocks via hybridization, and EGSs mediate enzymatic cleavage of the target RNA.” Brief, page 13. Appellants, at the same time, admit that “an antisense binding mechanism is required for the presently claimed method...” Id. Therefore, we agree with the examiner that appellants' alleged distinction is without a difference from the prior art, and that the examiner has provided a prima facie case of obviousness which remains unrebutted by appellants.

Appellants allege that the “combination of Shaji and Milligan do not provide for an enabling disclosure for identifying and producing a set of EGSs, that may be modified by PNAs, when in combination with the target RNA, provide a sufficient and specific substrate for RNAse P cleavage.” Brief, page 16.

The examiner responds, that “one of ordinary skill in the art would have had an expectation of success since the art has taught that these modifications have been used and provide for increased target affinity.” Answer, page 8. The examiner also notes that the appellants' specification provides no working examples of PNA modified EGS. Id.

For the reasons herein, we find no error in the examiner's conclusion that the subject matter of claim 36 is obvious in view of George and Milligan under 35 U.S.C. § 103(a) .

CONCLUSION

The rejection of claim 37 under 35 U.S.C. §102(b), as anticipated by George is affirmed. Claims 34 and 35 fall with claim 37. The rejection of claims 36 under 35 U.S.C. §103(a), as obvious over George in view of Mulligan is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

SHERMAN D. WINTERS Administrative Patent Judge	)
TONI R. SCHEINER Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
DEMETRA J. MILLS Administrative Patent Judge	)

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